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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/758,572	01/14/2004	Sharon Cohen-Vered	68518-A/JPW/GJG/JBC	5919

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EXAMINER	
DESAI, ANAND U	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/758,572	COHEN-VERED ET AL.	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,21,31,32,41-43,52,53 and 57-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,21,31,32,42,43,53 and 57-61* is/are rejected.

7)☒ Claim(s) *41 and 52* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to Amendment filed on September 29, 2005.

Election/Restrictions

2. Applicant's argument filed September 29, 2005 has been fully considered but they are not persuasive. The Examiner has cited U.S. Patent 6,407,079 B1 to disclose another method of producing a pharmaceutical composition comprising a sparingly water-soluble drug. Further, the method of alleviating the symptoms of systemic lupus can be practiced with another composition (see Office Action mailed June 6, 2005, 1st paragraph).

However upon further consideration, withdrawn claims 19, 21, 32, 41, 43, and 52 are rejoined with the product claims and are currently under examination, because it would not be an undue burden to search the method claims. Since all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, the restriction requirement made in the Office action mailed on August 25, 2004 is hereby withdrawn.

3. Claims 1-19, 21, 31, 32, 41-43, 52, 53, and 57-61 are currently pending and are under examination.

New Rejections and Objections

Specification

4. The disclosure is objected to because of the following informalities:

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 26, line 24. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Objections

6. Claims 41 and 52 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 21, 32, and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. In claim 21, in step a), what is the "predetermined concentration"?

10. In claims 32, and 43, in step a), how long is the temperature maintained at -40°C, and -45°C, respectively? In steps b), d), and e), what is the "predetermined time"? In step e), what is the reduced pressure that lyophilizes the pharmaceutical composition?

Claim Rejections - 35 USC § 103

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 19, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes U.S. 2004/0127408 A1 (Priority date = February 26, 2001) in view of Hora et al. U.S. Patent 5,997,856.

Mozes discloses peptides and pharmaceutical compositions for the treatment of systemic lupus erythematosus. Mozes discloses a 19-mer peptide sequence identified as SEQ ID NO: 6,

which has 100% identity with current application SEQ ID NO: 1 (see U.S. Publication '408, paragraphs 21, 67, and claims 2, and 9). Mozes does disclose the salt of the peptide, including an acetate salt (see U.S. Publication '408, paragraphs 15, 88, and claim 1). Mozes discloses a pharmaceutical composition comprising the peptide and a pharmaceutically acceptable carrier (see U.S. Publication, '408, claims 24, and 25). Mozes does not explicitly disclose a pharmaceutical composition comprising a pharmaceutically acceptable salt of a peptide and a substituted β-cyclodextrin.

Hora et al. disclose the solubilization and/or stabilization of polypeptides, especially proteins, using cyclodextrin selected from the group consisting of hydroxypropyl, hydroxyethyl, glucosyl, maltosyl, and maltotriosyl derivatives of β-cyclodextrin (see entire document, particularly col. 11, line 59 through col. 12, line 17). Hora et al. disclose protein, hydroxypropyl β-cyclodextrin compositions that have proteins at concentrations ranging from 0.25 mg/ml to 1 mg/ml (see U.S. Patent '856, col. 22, Table 2). Hora et al. describes the formulation of IL-2 recombinant protein with hydroxypropyl β-cyclodextrin in a 10 mM citrate buffer solution, with a pH of 6.5 (see U.S. Patent '856, col. 20, lines 30-33, and col. 22, Table 2, column describing multiple protein formulations).

One would have been motivated to manufacture the pharmaceutical composition comprising an aqueous carrier, a pharmaceutical acceptable salt of the peptide disclosed by Mozes with the β-cyclodextrin derivatives disclosed by Hora et al., because of the enhanced solubilization and stabilization of the peptide in the β-cyclodextrin derivative solution. Therefore, it would have been obvious to the person having ordinary skill in the art to manufacture the pharmaceutical composition comprising an aqueous carrier, a pharmaceutical

acceptable salt of the peptide identified as SEQ ID NO: 1 that is disclosed by Mozes, along with the β-cyclodextrin derivatives disclosed by Hora et al. to treat systemic lupus erythematosus (current application, claims 19, and 21).

Maintenance of Rejections

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ormum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-18, 31, 42, 53, and 57-61 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13, 24, 25, 37, 48, and 52 of copending Application No. 10/758,397 (U.S. Patent Application Publication 2005/0008634 A1).

14. The provisional obviousness-type double patenting rejection is disclosed in the office action mailed June 6, 2005.

Claim Rejections - 35 USC § 103

15. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

16. Claims 1-4, 7, 8, 11, and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes U.S. 2004/0127408 A1 (Priority date = February 26, 2001) in view of Hora et al. U.S. Patent 5,997,856.

17. Claims 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes U.S. 2004/0127408 A1 (Priority date = February 26, 2001) in view of Hora et al. U.S. Patent 5,997,856 as applied to claim 1-4, 7, 8, 11, 31, 42, 53, 57, and 59-61 above, and further in view of Anderson, B.D. and Flora, K.P (Chapter 34, pages 739-754, The Practice of Medicinal Chemistry, edited by Camille Georges Wermuth, Academic Press 1996).

18. Claims 9, 10, and 12-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mozes U.S. 2004/0127408 A1 (Priority date = February 26, 2001) in view of Hora et al. U.S. Patent 5,997,856 as applied to claim1-4, 7, 8, 11, and 31 above, and further in view of Stella et al. U.S. Patent 5,134,127.

19. The 103(a) rejections are disclosed in the office action mailed June 6, 2005.

Response to Remarks

20. Applicant's state the motivation to combine Mozes (U.S. Publication 2004/0127408 A1) and Hora et al. (U.S. Patent '856) is lacking. Applicant's state absent hindsight, there is no reason of record motivating the combination of the salt of the peptide of Mozes with any solubility enhancer, much less the ones of the U.S. Patent '856. Applicant's further state even if the solubility of the salt of the peptide was known to be a problem, there is no reason of record to select a β-cyclodextrin from the large number of known solubility enhancers. Applicant's state

there is no expectation of success if Mozes and U.S. Patent '856 are combined. Applicant's further state the remaining 103(a) rejections all suffer from the same deficiencies as discussed in the Mozes in view of Hora et al. (U.S. Patent '856) response, and the other references fail to remedy any of the deficiencies. Applicant's arguments filed September 29, 2005 have been fully considered but they are not persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, Mozes does disclose an invention that provides a pharmaceutical composition comprising at least one peptide polymer and a pharmaceutically acceptable carrier, wherein the pharmaceutical composition is particularly useful for the treatment of SLE and amelioration of the clinical manifestations of the disease (encompassing a salt of SEQ ID NO: 6, see [0015], [0021], [0022], [0061], and [0067]). Mozes does disclose modification of the pharmaceutical properties of the peptide, such as solubility (see [0088]). Hora et al. (U.S. Patent '856) does disclose the solubilization and/or stabilization of polypeptides using cyclodextrins (see col. 11, line 59 – col. 12, line 17). Hora et al. does disclose the state of the art by describing multiple proteins solubilzed in a concentration range from 0.25 mg/ml to 1 mg/ml with hydroxypropyl β-cyclodextrin (see col. 22, Table 2), and also describes the use of polypeptides

for treatment of disease (col. 12, line 41-52). Therefore, a person having ordinary skill in the art would have been motivated to solubize the salt of the peptide disclosed by Mozes with the substituted β-cyclodextrin disclosed by Hora et al. and would have expected to succeed in solubilizing the pharmaceutical composition because Hora et al. has disclosed the state of the art of successfully solubilizing multiple polypeptides.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Anderson et al. describe the ideal pH for a pharmaceutical composition (see Office action mailed June 6, 2005). Therefore, a person having ordinary skill in the art would have been motivated and expected to succeed in manufacturing a pharmaceutical composition with the disclosed physiological pH. Stella et al. (U.S. Patent '127) does disclose the enhanced solubilization, and reduced toxicity of sulfoalkyl ether cyclodextrin derivatives for pharmaceuticals (see Office Action mailed June 6, 2005). Therefore, a person having ordinary skill in the art would have been motivated and expected to succeed in manufacturing a pharmaceutical composition with a sulfobutyl ether substituted β-cyclodextrin.

Furthermore, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge

gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

21. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 7:00 a.m. - 3:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

December 20, 2005

JON WEBER
SUPERVISORY PATENT EXAMINER